UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,082	07/21/2006	Anton Mayr	BN55-PCT-US	6952

76392 7590 06/13/2008

LAW OFFICE OF SALVATORE ARRIGO
1050 CONNECTICUT AVE. NW
10TH FLOOR
WASHINGTON, DC 20036

EXAMINER	
BLUMEL, BENJAMIN P	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
06/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,082	MAYR ET AL.	
	Examiner	Art Unit	
	BENJAMIN P. BLUMEL	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *70-95* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants are informed that the rejections of the previous Office action not stated below have been withdrawn from consideration in view of the Applicant's arguments and/or amendments.

Claims 70-95 are examined on the merits. All previously presented claims have been cancelled.

Response to Arguments

Applicant's arguments filed February 25, 2008 have been fully considered but they are not persuasive. See responses below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(New Rejection Necessitated by Amendments) Claims 82 and 83 are rejected under 35 U.S.C. 102(b) as being anticipated by McCabe et al. (Vaccine, 2002).

A method for producing a paramunity inducer, comprising:

(a) isolating a myxomavirus from infected tissue of a rabbit;

(b) adapting the virus to a permissive cell system; and

(c) passaging the adapted virus to generate an attenuated myxomavirus that induces paramunity, wherein the attenuated myxomavirus has lost the receptor properties of one or more myxomavirus interferon receptor, one or more myxomavirus tumor necrosis factor receptor, and one or more myxomavirus interleukin receptor. Some examples of these receptors are IFNa-R, IFNy-R, TNF-R, IL-1-R, IL-2-R, IL-6-R and IL-12-R. However, the active steps of the claimed method are: (a) isolating a myxomavirus from an infected tissue of a rabbit; (b) adapting the virus to a permissive cell system; and (c) passaging the adapted virus resulting in an attenuated myxomavirus. Therefore, teachings of McCabe et al. still anticipate the instant invention because they teach the active steps of isolating a myxoma virus from rabbits and its subsequent adaption/attenuation by serial passaging in Rabbit Kidney cells (RK-13). Therefore McCabe et al.'s active steps are the same as the instant invention and would be expected to generate a virus with the same mutations. See page 2455.

(New Rejection Necessitated by Amendments) Claims 82-84 are rejected under 35 U.S.C. 102(b) as being anticipated by Saito et al. (Journal of Infectious Diseases, 1964).

A method for producing a paramunity inducer, comprising:

(a) isolating a myxomavirus from infected tissue of a rabbit;

(b) adapting the virus to a chorioallantoic membrane of an incubated chicken eggs; and

(c) passaging the adapted virus to generate an attenuated myxomavirus that induces paramunity, wherein the attenuated myxomavirus has lost the receptor properties of one or more myxomavirus interferon receptor, one or more myxomavirus tumor necrosis factor receptor, and one or more myxomavirus interleukin receptor. Some examples of these receptors are IFNa-R,

IFNy-R, TNF-R, IL-1-R, IL-2-R, IL-6-R and IL-12-R. However, the active steps of the claimed method are: (a) isolating a myxomavirus from an infected tissue of a rabbit; (b) adapting the virus to a permissive cell system; and (c) passaging the adapted virus resulting in an attenuated myxomavirus. Therefore, the teachings of Saito et al. still anticipate the claimed invention, even though they do not disclose receptor modifications, since they teach the attenuation of two myxoma virus strains (isolated from rabbits) by adapting the viral isolates through serial massaging in the chorioallantoic membrane of White Leghorn Hen eggs followed by serial passaging in rabbit kidney cells. Therefore Saito et al.'s active steps are the same as the instant invention and would be expected to generate a virus with the same mutations. See page 418.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

(New Rejection Necessitated by Amendments) Claims 70-75, 80, 81, 85-88, 94 and 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayr (US 2003/0013190 A1) in view of Saito et al. (*supra*) and Paoletti (US Pat 6,340,462).

In addition, the claimed invention is drawn to either the passaging of the adapted virus in a binary cell culture or in Vero monkey cells at least 80, 120 or 150 times. The attenuated virus is also inactivated by exposure to 0.01-1.0% of beta-propiolactone.

Mayr teaches the further attenuation of MVA which was previously adapted by culturing in chicken eggs at the chorioallantoic membrane and initially attenuated with numerous passages in CEFs. Mayr achieves this further attenuation by passaging MVA in Vero cells 100 times and 200 times thus producing Vero-MVA-100 and Vero-MVA-200, respectively. However, Mayr doesn't teach the attenuation of *myxoma virus* or its inactivation with beta-propiolactone at a concentration of 0.01%-1%. See columns 11 and 12.

The teachings of Saito et al. are discussed above.

Paoletti teaches the use of 0.001% beta-propiolactone to inactivate recombinant fowlpox, a species related to myxomavirus (another orthopoxirus). See columns 11 and 12.

It would have been obvious to one of ordinary skill in the art to modify the methods taught by Mayr in order to attenuate *Myxoma virus* in Vero cells. One would have been motivated to do so, given the suggestion by Mayr that the method be used to attenuate MVA (a member of the same family as *Myxoma virus*. There would have been a reasonable expectation of success, given the knowledge that *Myxoma virus* can be attenuated following adaptation in chicken eggs and serial passage in RK cells, as taught by Saito et al. and also given the knowledge that inactivation of other poxviruses can be achieved with 0.001% of beta-

propiolactone, as taught by Paoletti. Even though Paoletti did not use the claimed concentration range, determining such a range is part of routine optimization, which does not constitute novel or unobvious characteristics, MPEP § 2144.05. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to arguments:

Applicant's state that their new claims 82-95 which recite, "…attenuated myxomavirus has lost the receptor properties of one or more myxomavirus interferon receptor, one or more myxomavirus tumor necrosis factor receptor, and one or more myxomavirus interleukin receptor." are not disclosed in Mayr. In response, even though Mayr does not teach these limitations, the active steps of Saito et al. are the same as that of the instant invention, and therefore, the virus produced by Saito et al. would be expected to inherently possess these altered characteristics.

(New Rejection Necessitated by Amendments) Claims 70-75, 80-89, 94 and 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayr (*supra*) in view of Saito et al. (*supra*), Paoletti (*supra*) and Ogino et al. (Journal of Virology, 2004).

The claimed invention is also drawn to the use of a binary cell culture to passage viruses in which two cells are fused.

The teachings of Mayr, Saito et al. and Paoletti are discussed above, however they do not teach passaging viruses in cells that are fused.

Ogino et al. teach the passaging of Hantaan virus in Vero E6 cells that fuse with infected and uninfected cells. See page 10777.

It would have been obvious to one of ordinary skill in the art to modify the methods taught by Mayr in order to attenuate *Myxoma virus* in Vero cells or cells fused with other cells. One would have been motivated to do so, given the suggestion by Mayr that the method be used to attenuate MVA (a member of the same family as *Myxoma virus*. There would have been a reasonable expectation of success, given the knowledge that *Myxoma virus* can be attenuated following adaptation in chicken eggs and serial passage in RK cells, as taught by Saito et al., also given the knowledge that inactivation of other poxviruses can be achieved with 0.001% of beta-propiolactone, as taught by Paoletti and also given the knowledge that viruses can be cultured in Vero cells that fuse with other cells, as taught by Ogino et al. Even though Paoletti did not use the claimed concentration range, determining such a range is part of routine optimization, which does not constitute novel or unobvious characteristics, MPEP § 2144.05. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(Prior Rejection Maintained) Claims 76-79 and 90-93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants argue that since the specification on pages 8-9 teach how to fuse CEFs to VERO cells and that cell fusion is widely known in the art, their claimed AVIVER cell is readily obtainable and therefore does not have to be deposited.

In response, the Office acknowledges that CEFs and VERO cells, the starting materials for the cell fusion process, are available. The Office also acknowledges that the technique(s) of cell fusion is widely known in the art. However, Applicant is claiming a particular cell by name, and that exact cell must be known and publicly available. While one skilled in the art would be able to generate a cell that is similar in structure and function to the AVIVER cell, one would not be able to generate the identical cell as is instantly claimed. If Applicant wishes to claim the cell by name (laboratory designation), the rejection will be maintained because the requirements of being known and publicly available must be met in order to overcome the rejection. Therefore, the rejection is maintained for reasons of record.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 70-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 70 recites, "…passaging the adapted virus in a binary cell culture…", however, claim 72 recites, "…passaging of the adapted virus comprises passaging the virus in Vero monkey kidney cells." Therefore, it is unclear if the adapted virus is passaged in a binary cell culture or in a Vero cell culture. Claims 71 and 73-81 are rejected since they depend from claims 70 or 72.

Summary

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stacy B Chen/
Primary Examiner, Art Unit 1648

/BENJAMIN P BLUMEL/
Examiner
Art Unit 1648